AMRL-TDR-64-74

THE EFFECT OF DECABORANE INJECTION ON MACACA MULATTA AND MACACA IRUS OPERANT BEHAVIOR

HERBERT H. REYNOLDS, MAJOR, USAF
HENRY W. BRUNSON, A2C, USAF

6571st AEROMEDICAL RESEARCH LABORATORY
HOLLOMAN AIR FORCE BASE, NEW MEXICO

KENNETH C. BACK, PhD
ANTHONY A. THOMAS, MD

AEROSPACE MEDICAL RESEARCH LABORATORIES
WRIGHT-PATTERSON AIR FORCE BASE, OHIO

AUGUST 1964

BIOMEDICAL LABORATORY
AEROSPACE MEDICAL RESEARCH LABORATORIES
AEROSPACE MEDICAL DIVISION
AIR FORCE SYSTEMS COMMAND
WRIGHT-PATTERSON AIR FORCE BASE, OHIO

NOTICES

When US Government drawings, specifications, or other data are used for any purpose other than a definitely related government procurement operation, the government thereby incurs no responsibility nor any obligation whatsoever; and the fact that the government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data is not to be regarded by implication or otherwise, as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto.

Qualified requesters may obtain copies from the Defense Documentation Center (DDC), Cameron Station, Alexandria, Virginia 22314. Orders will be expedited if placed through the librarian or other person designated to request documents from DDC (formerly ASTIA).

Do not return this copy. Retain or destroy.

Stock quantities available at Office of Technical Services, Department of Commerce, Washington, D. C. 20230.

Change of Address

Organizations receiving reports via the 6570th Aerospace Medical Research Laboratories automatic mailing lists should submit the addressograph plate stamp on the report envelope or refer to the code number when corresponding about change of address.

The experiments reported herein were conducted according to the "Principles of Laboratory Animal Care" established by the National Society for Medical Research.

800 - October 1964 - 448 - 7-225

THE EFFECT OF DECABORANE INJECTION ON MACACA MULATTA AND MACACA IRUS OPERANT BEHAVIOR

HERBERT H. REYNOLDS, MAJOR, USAF
HENRY W. BRUNSON, A2C, USAF
KENNETH C. BACK, PhD
ANTHONY A. THOMAS, MD

FOREWORD

This experimentation, which began on 10 February 1964 and was completed on 24 February 1964, was performed jointly by members of the 6571st Aeromedical Research Laboratory, Holloman AFB, New Mexico, and the Aerospace Medical Research Laboratories, Wright-Patterson AFB, Ohio. The research was conducted in support of Project 6302, "Toxic Hazards of Propellants and Materials," Task 630202, "Pharmacology-Biochemistry," for the Toxic Hazards Branch, Physiology Division, Biomedical Laboratory, Aerospace Medical Research Laboratories. The assistance of the following persons is gratefully acknowledged.

Mr. Jack Sadler	Subject monitoring and data acquisition.
Mr. Richard Williams	Subject monitoring and data acquisition.
Capt. V. L. Carter, VC	Injections and subject health status.

This technical report has been reviewed and is approved.

C. H. KRATOCHVIL
Major, USAF, MC
Commander
6571st Aeromedical Research Laboratory

WAYNE H. McCANDLESS
Technical Director
Biomedical Laboratory

ABSTRACT

Ten adult monkeys, eight on negatively reinforced (low level shock) tasks and two on positively reinforced (food reward) tasks, were injected with either 2 mg, 4 mg, or 1 mg followed by 2 mg decaborane per kg body weight, and their performance on various operant tasks was compared with baseline performance. All animals exhibited a performance decrement on at least one task, with 75% of the subjects exhibiting a decrement on the remaining tasks. In over half the cases performance changes preceded clinical symptoms. There was no significant difference between the 2 mg and 4 mg exposures when a subject showed a decrement on negatively reinforced tasks. However, those subjects that received 1 mg followed the next day by 2 mg (positively reinforced animals) did not noticeably improve or return to baseline for a much longer period than the 2 mg and 4 mg groups (negatively reinforced).

Subjects exposed to levels of decaborane such as those employed in this research may be expected to exhibit a performance decrement or clinical symptoms during the first fifty hours, since one or the other will probably occur during that time period. Usually, the first indication will be a performance decrement on a task requiring continuous motor behavior or a series of discriminations within the first 30 hours. Tasks of a discrete nature may, at lower exposure levels, reflect no decrement and, in these instances, there may also be a total absence of clinical symptoms. When performance decrements do take place, one may expect a return to baseline between 3 and 10 days.

LIST OF CONTENTS

LIST OF ILLUSTRATIONS

LIST OF TABLES

THE EFFECT OF DECABORANE INJECTION ON MACACA MULATTA AND MACACA IRUS OPERANT BEHAVIOR

I. INTRODUCTION

The boron hydrides (boranes) which, according to Rozendaal (ref 8), were first described in 1879, have been given much attention for the past 20 years, particularly during the last decade. With the advent of the space age, the boranes have been used extensively as high energy fuels (HEFs). The toxicology and toxicity of these compounds have been studied by numerous investigators (ref 1-16). Their research has revealed that borane toxicity produces central nervous system symptoms in the form of headaches, depression, muscular fasciculations, lack of awareness, and even catatonic stupors. Differential electroencephalograms have been shown for certain brain areas via deep electrode placements (ref 2), and in human exposures marked personality changes have been observed.

Although a great deal of research on the pharmacology, toxicity, and clinical manifestations of the boranes has been accomplished, no one has studied the effects on learned behavior (performance). Therefore, the purpose of this investigation was to evaluate animal performance following injection of decaborane. Decaborane, $B_{10}H_{14}$, is a white crystalline material, soluble in olive or cottonseed oil (but not in water) and is rapidly absorbed by inhalation or through the skin.

II. METHOD

A. Subjects

The subjects were 10 adult Macaque monkeys (Macaca Mulatta and Macaca Irus), weighing between 4.32 and 7.39 kg. All monkeys had been trained on the performance tasks to a stabilized level over a period of several months. Subjects 22 and 23 were not trained on the auditory monitoring task.

B. Apparatus

The apparatus was composed of two major items: a work chamber, especially designed for psychopharmacological research, and a rack of electronic relay circuitry for programing the performance tasks (fig. 1). The inside dimensions of the work area of the chamber were 24 by 24 by 26 inches, and the performance panel measured 13.5 by 14 inches. The performance panel included two stimulus lights and two response levers, one set mounted on each side of an auditory stimulus-response key. The stimulus-response key contained 0.125-inch diameter holes to permit the presentation of a tone from a speaker mounted behind it. A red lamp was mounted above the right lever as a cue for a continuous avoidance task, and a blue lamp, above the left lever, as a cue for a discrete avoidance task.

C. Performance Schedule

The schedule was of 15 minutes duration and was comprised of three integrated tasks. At the onset of the red lamp above the right lever, the subject had to press the lever at least once every 15 seconds for the full 15 minutes. If the monkey failed to respond as often as required it received a mild shock to the soles of its feet. Since the subject diligently presses the lever to insure against shock this task has been labeled continuous avoidance (CA). Throughout the 15-minute work period the blue lamp above the left lever was turned on at 2, 5, 8, 11, and 14 minutes and the subject was required to turn the lamp off by pressing the corresponding lever within two seconds (discrete avoidance - DA). Failure to respond within the specified time period resulted in a mild shock to the soles of the feet. The third task of the performance schedule was an auditory monitoring (AM) task, which also ran concurrently with CA and involved the presentation of a 1024 cps tone at 80 db from the speaker described in section B. Presentations of the auditory stimulus occurred at 3.5, 5, 7.5, 11, and 13.5 minutes, and the subject was required to turn the tone off by pressing the response key within 2 seconds. Failure to respond within the allotted time resulted in a mild shock to the soles of the feet.

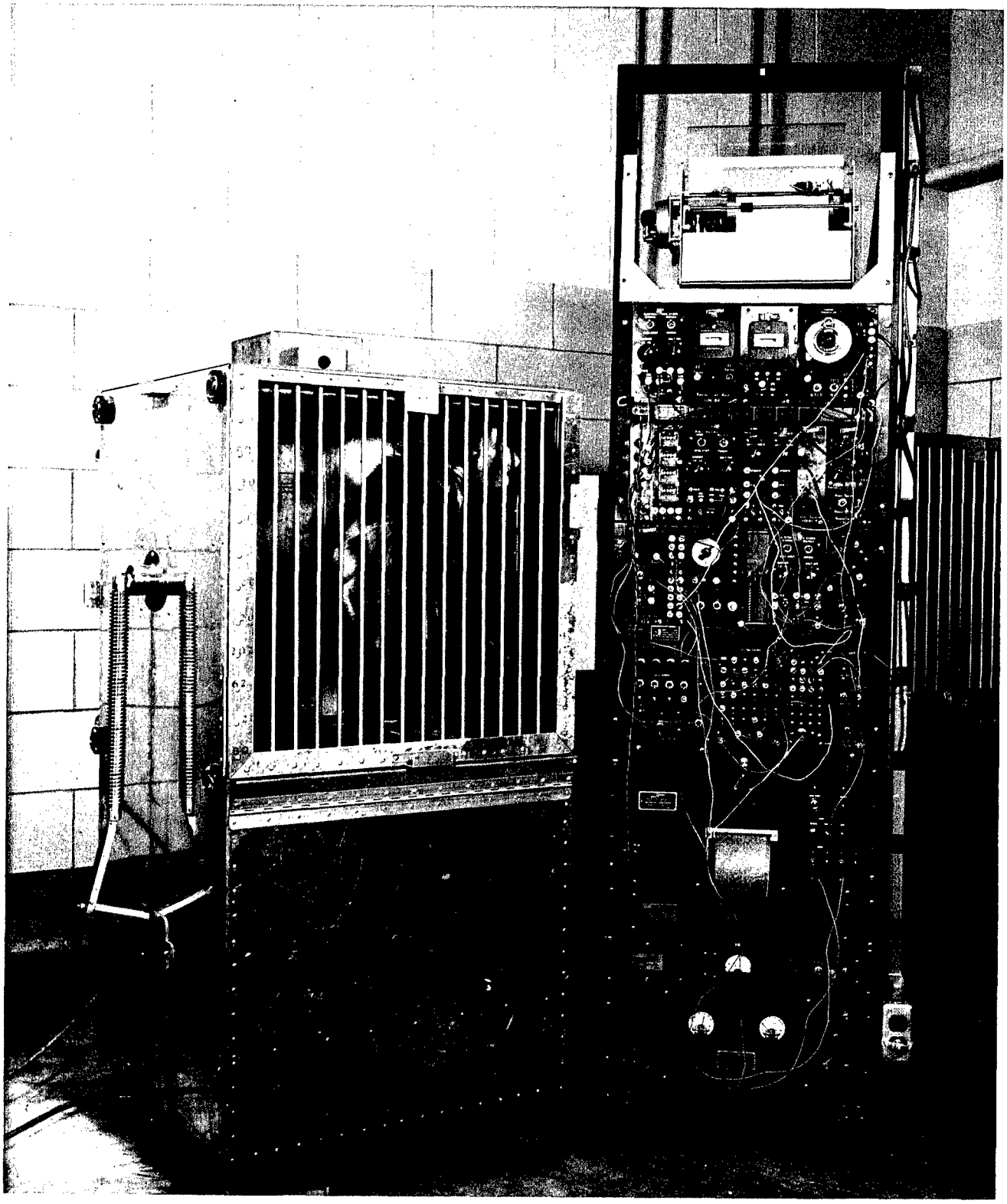

Figure 1. Work Chamber and Programing Rack

D. Procedure

The subjects were divided into two groups of four each based on level of performance and comparable body weight. After being restrained in squeeze cages, the subjects were injected with either 2 or 4 mg decaborane per kg of body weight as indicated in table I.

TABLE I

Injection Protocol

Group I

(2 mg decaborane per kg body weight)

Subject No.	Subject Weight (kg)	Time of Injection
4	5.05	0815
9	4.89	0825
22	6.48	0835
2	5.45	0845

Group II

(4 mg decaborane per kg body weight)

Subject No.	Subject Weight (kg)	Time of Injection
8	4.32	0820
23	6.70	0830
15	6.82	0840
7	7.39	0850

At 0900 subjects 4 and 9 (group I) and subjects 8 and 23 (group II) began the 15-minute performance program and continued on the hour, i.e. 1000, 1100, etc. for a total of eight sessions each day throughout the experiment. At 0930 subjects 2 and 22 (group I) and subjects 7 and 15 (group II) also began the performance program and continued on the half hour, i.e. 1030, 1130, etc for eight sessions each day throughout the experiment. Each animal served as its own control since pre-experimental task performance was sufficiently stabilized for each subject.

Two additional monkeys were injected with 1 mg decaborane per kilogram at 0855 and 0900 on the same day as the other eight monkeys, and with 2 mg per kg the following day at the same times. These two subjects were trained on positively reinforced (food pellets) discrimination tasks, primarily to evaluate decaborane effects on the hunger drive. Since the major concern in any high risk situation for humans is the ability of an individual to act on his environment in promoting safety and survival, it was considered important to compare motivational levels under both positive and negative reinforcement conditions. If an animal subject is capable of carrying out a learned task under positive reinforcement conditions but does not do so simply because his hunger drive is diminished, then an accurate evaluation of performance changes due to sensory-motor incapacitation is not possible. On the other hand, if motivation is strong enough (avoidance of pain), then the animal subject should make every possible effort to perform at his highest level of capability. Data on the outcome of this ancillary aspect of the experimentation are presented in the Results and Discussion-Conclusions Sections.

III. RESULTS

The results can be best presented by referring to each of the subjects separately. Qualitative and quantitative subject differences preclude a meaningful group approach.

A. Group I (2 mg decaborane per kg body weight)

Subject No. 2

Summary of Performance

CA performance was somewhat depressed from the very beginning, but did not drop below baseline until the 48th hour. At the 144th hour following injection, the subject evidenced a definite improvement in performance, then declined somewhat at the 151st hour. At the 170th hour the subject returned to and continued to maintain his baseline CA performance. The compound appeared only to reduce the overall level of CA responding, and at no time throughout the 8 days of testing was this subject impaired to the point of being unable to respond. DA and AM performance were virtually unaffected during the entire experiment. Figure 2 provides a graphic presentation of the significant performance changes when compared with baseline data.

Pertinent Observations

No clinical symptoms.

Subject No. 4

Summary of Performance

CA performance fell immediately below baseline following injection, but returned briefly to baseline level at the 6th and 8th hours and again at the 26th-28th hours. A significant decrement occurred simultaneously on all tasks between the 29th and 31st hours and the subject became completely impaired at the 51st hour. At the 122nd hour the subject began to perform again and evidenced a noticeable improvement on all three tasks between the 124th and 126th hours. Performance returned to and was maintained at baseline level on all tasks beginning at the 144th hour. Figure 3 provides a graphic presentation of the significant performance changes when compared with baseline data.

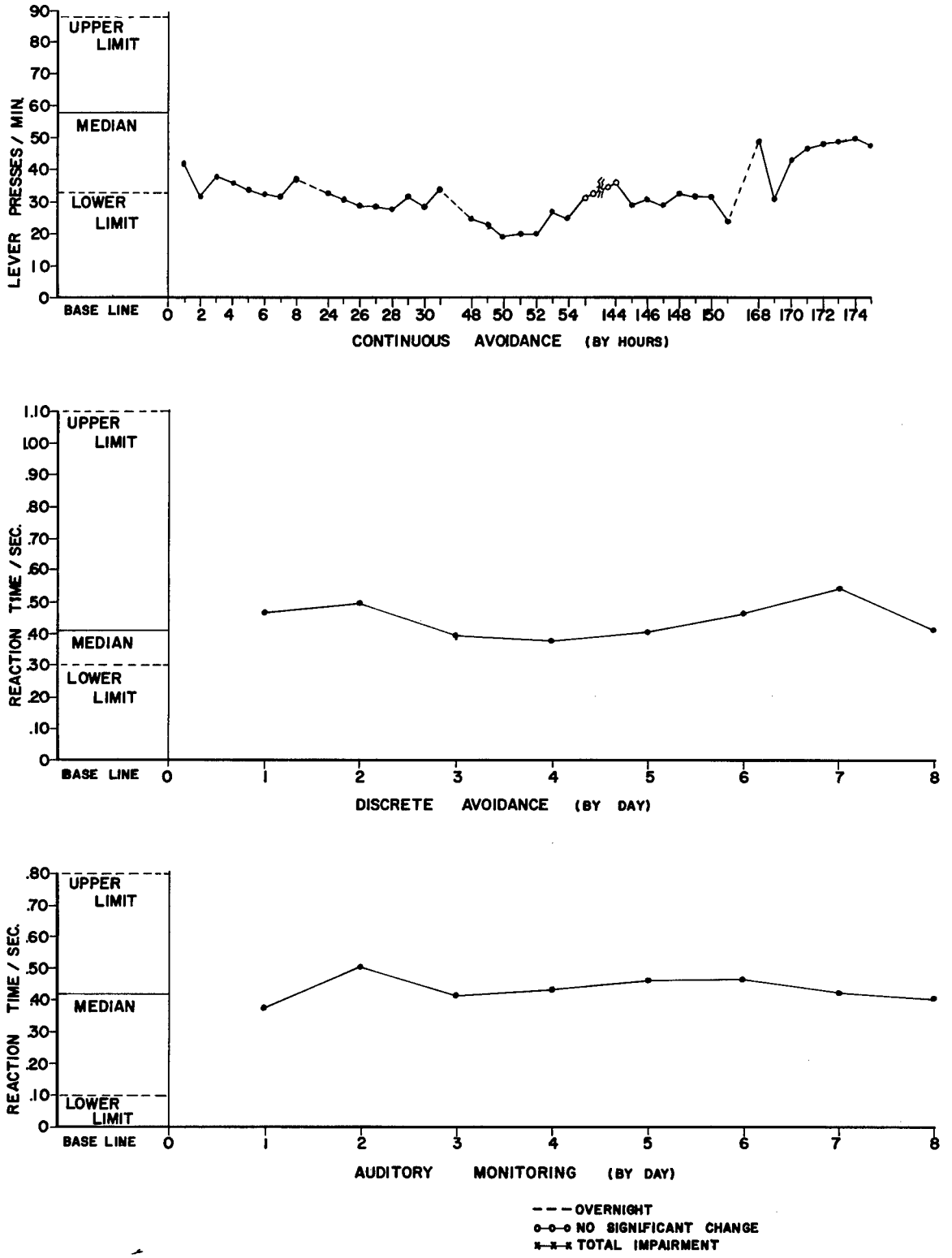

Figure 2. Baseline and Experimental Performance, Subject No. 2

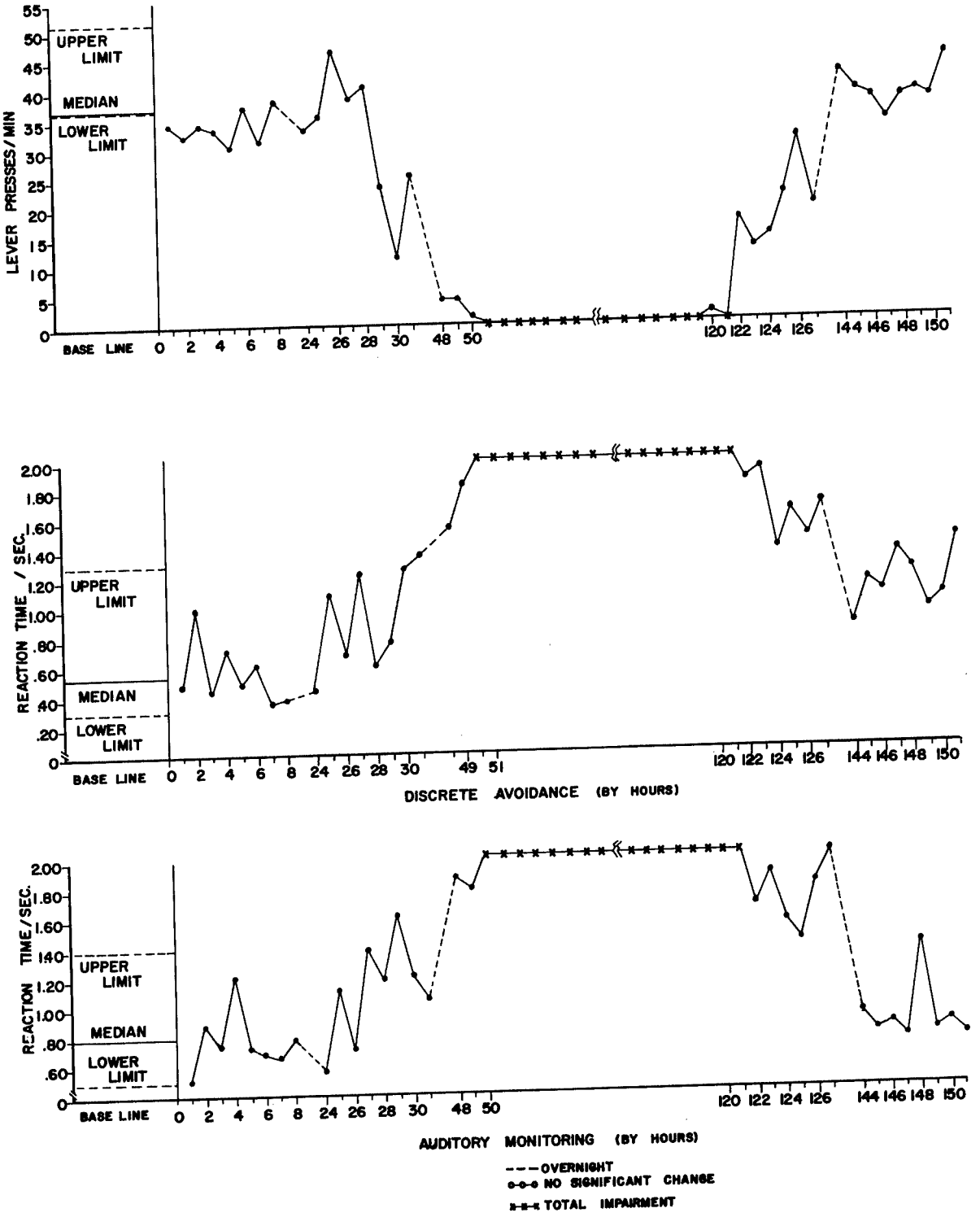

Figure 3. Baseline and Experimental Performance, Subject No. 4

Pertinent Observations

Day 2

0845 - Lying in bottom of cage during rest period (almost in the prone position). Subject decidedly lethargic.

1105 - Started shaking cage bars until he took some shocks for nonperformance. Subject is working in spurts.

1355 - Circling cage and bending over and then raising up in an atypical fashion.

1400 - Subject is now showing a decided performance decrement on CA. He appears to be doing an adequate job on DA and AM, but CA behavior is essentially lost.

Day 3

1005 - Is looking back and forth above his head as if "watching a movie" on the ceiling of the cage. Works occasionally and vocalizes when shocked. Performance impaired but subject is alert. Continues to have what appear to be hallucinations.

1330 - Gazes at the ceiling of his cage and rolls his head from side to side intermittently. He then puts his head down and curls up for long periods as if in a catatonic state.

Day 4

0800 - Walks around the cage in circles looking down through the bars as if trying to find something. He has slight muscular fasciculations and his head is bobbing similar to a "Parkinsonian." Complete confusion concerning his environment.

Day 5

0800 - Very reluctant to enter work chamber. Has muscular tremors in rhythm with respiration. Little awareness, will not work. Ate almost no fruit last night.

1321 - Given 2-1/2 mg of Ephedrin sulfate (1/2 mg/kg) ip.

1600 - Is huddled over and withdrawn at the end of the "work" day.

Day 6

0815 - Has improved since yesterday.

0930 - Is in poorer condition now than he was during the 1st work session from 0800-0815.

1000 - Apparently still in bad shape. Urinated and defecated profusely after he took his first shock at the beginning of this session. Not responding at all at first.

Day 7

1600 - Has returned to baseline level of performance (during past 8 hours work) and will no longer continue in the testing program.

Subject No. 9

Summary of Performance

Performance was never completely impaired and only CA performance reflected a decrement during the experiment. CA performance fell below baseline only at the 31st, 48th, 52nd and 77th hours. At the 78th hour the subject returned to and maintained baseline level performance. Figure 4 provides a graphic presentation of the significant performance changes when compared with baseline data.

Pertinent Observations

No clinical symptoms.

Subject No. 22

Summary of Performance

Performance took an early downward trend following injection. CA performance fell below baseline level at the 24th hour and DA at the

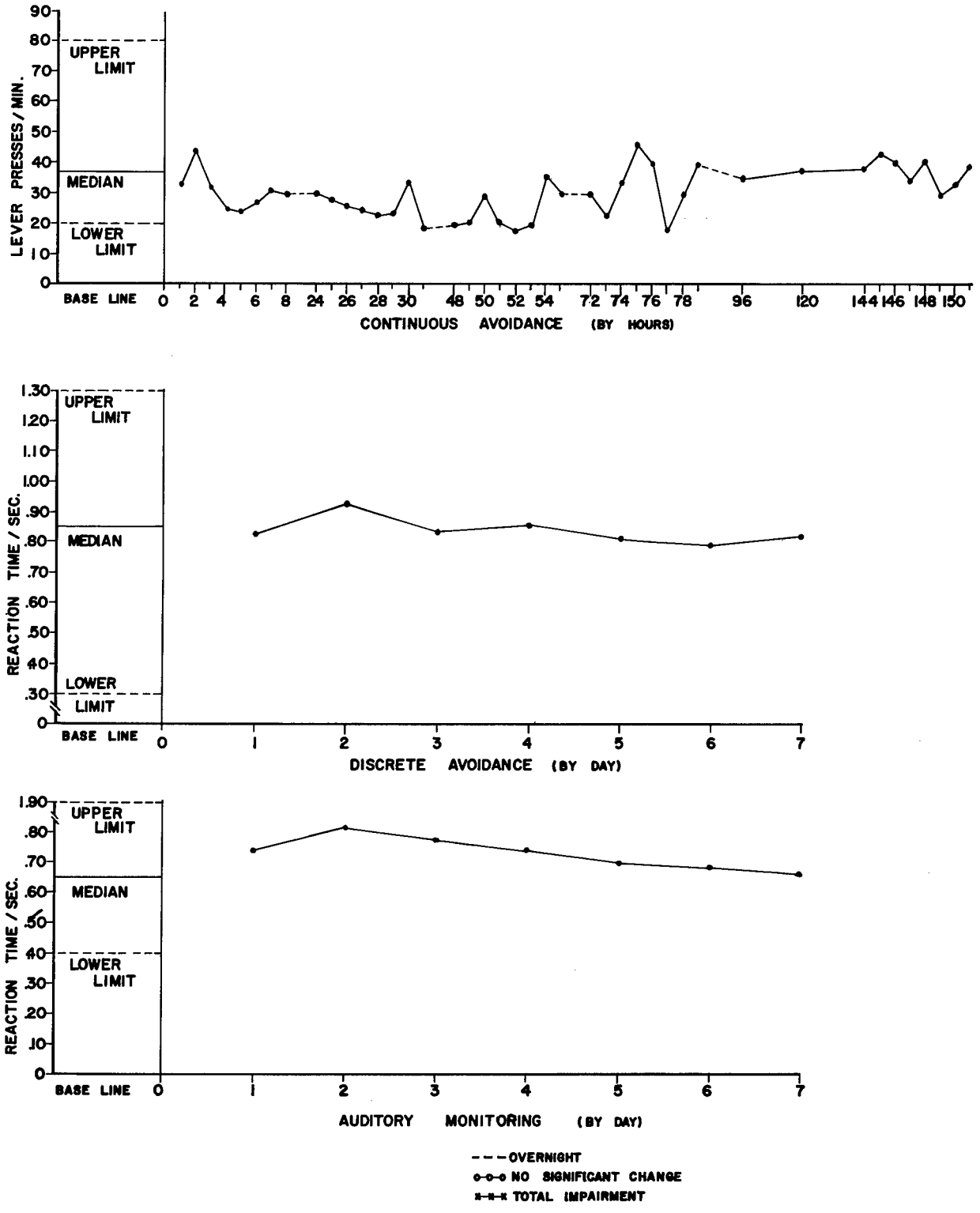

Figure 4. Baseline and Experimental Performance, Subject No. 9

28th hour. At the 30th hour performance became completely impaired and the subject did not respond again until the 96th hour. At the 96th hour the subject returned to his DA baseline performance level but at the 103rd hour became impaired once again and did not recover completely until the 120th hour. CA performance also returned to baseline level at the 120th hour, but from the 168th-240th hours performance remained slightly below baseline. After the 240th hour performance at baseline level was maintained. Figure 5 provides a graphic presentation of the significant performance changes when compared with baseline data.

Pertinent Observations

Day 1

1645 - Showed a downward trend from the 3rd to the 8th hours of performance which was not at all characteristic of this subject.

Day 2

0855 - Is very aggressive and hits the cage hard when approached; however, he has cut his CA lever presses down to 32 per minute from the previous low of 53 per minute.

1200 - Showed a decided performance decrement on the CA variable during the 1145-1200 work session. He took 15 CA shocks and his response rate was about 25% of his lowest pre-experimental level. He beat his head against the wall and was very disturbed (first clinical signs).

1352 - Started to bite chunks of flesh and hair out of his forearms. He sits and chews these chunks as if he were in no pain whatsoever.

1400 - Continuing to bite chunks out of his arms and legs.

1402 - Removed from work situation and placed in an open wire cage for observation and then further placed in a restraint chair.

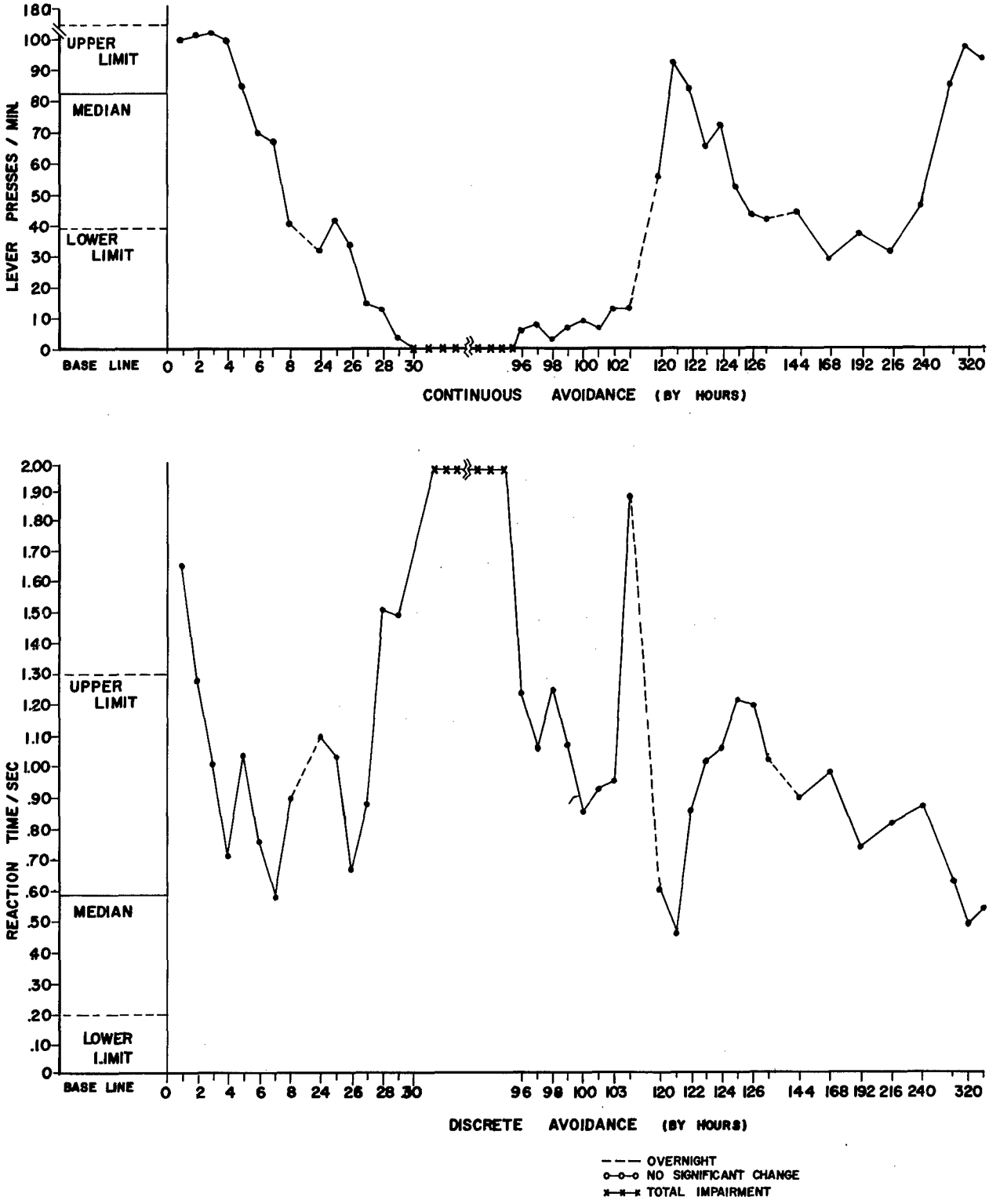

Figure 5. Baseline and Experimental Performance, Subject No. 22

1900 - Is in a plexiglass restraint chair to keep him from biting himself, looks ill but took some water (about 40 cc) from a cup and ate some banana.

2230 - Still looks bad, but his neck plate looked too tight and was loosened. The animal appeared to begin to breathe better immediately.

Day 3

0400 - Looks like he will "make it." He is more alert to noises and is moving about a bit more (from side to side).

0630 - Took some water (about 30 cc), a little banana, and is alert. Seems to prefer turning to his left each time his body is moved to a frontward facing position.

0800 - Placed into work chamber.

0830 - Is in various stages of catatonic behavior with periods of lucidness. Can be aroused at times but may revert to a prone position immediately. During the first work session at 0830 did not work although he was apparently aware of the stimulus lights and reacted vociferously to the shock.

0955 - Is in a depressed head-stand position.

1005 - Is not working and is just observed for periods of lucidity.

1330 - Is in a head-down, catatonic state.

Day 4

0800 - Will react to external stimulus but will not move from sitting position. Removed from work chamber.

Day 5

0800 - Transferred readily from transfer cage to work chamber but is withdrawn. Worked a little the first performance session from 0800-0815. Got all 5 DA's and has 84 lever presses on CA.

0945 - Is improved.

1230 - Continues to show improvement. His performance this last hour was indicative of greatly improved functioning.

Day 6

0955 - Performance still improving - decidedly better than the first work session this morning.

Day 9

1315 - Seems to be "improving," then gets "worse" - he is fluctuating and is still below baseline performance.

1600 - Still below his baseline performance level and will continue work tomorrow.

Day 10

0800 - Entered his work chamber readily and looks clinically sound.

1600 - Will continue until his performance is considered "typical."

Day 11

1600 - Is functioning at a very stable level and the experimenters are of the opinion that the subject has recovered from the effects of the decaborane.

B. Group II (4 mg decaborane per kg bodily weight)

Subject No. 7

Summary of Performance

This subject exhibited the most dramatic decrement and recovery of any of the eight subjects. Performance on all tasks fell below baseline at hour 25 and the next hour became completely impaired. On the last work session of day 6 (hour 128) the subject did not respond at all, but at the first session the next morning (hour 144) he performed at baseline level on all tasks and maintained this level

throughout the day. Figure 6 provides a graphic presentation of the significant performance changes when compared with baseline data.

Pertinent Observations

Day 1

0945 - Showing signs of nausea (frothing and slight vomiting), but performing well within baseline on all tasks.

1045 - Continues to show signs of nausea (frothing and slight vomiting) - performed within baseline on all tasks.

1148 - Continues to show signs of nausea (gagging and slight vomiting) - performed within baseline on all tasks.

1155 - Did not react readily to an implied threat and was not at all alert.

1217 - Exhibited mild emesis.

1256 - Exhibited mild emesis after working - performed within baseline on all tasks.

1322 - Exhibits emesis.

1349 - Exhibited emesis, sat with his head on hind leg and eyes closed, but responds to noises - performed within baseline on all tasks.

1419 - Exhibits emesis. Performed within baseline on all tasks.

1520 - Exhibits emesis.

1548 - Sleepy after 1530-1545 work session - performed within baseline on all tasks.

Day 2

0845 - Performance within baseline limits.

0915 - Is sitting in a fixed position and appears sleepy but is easily alerted by noise or movement.

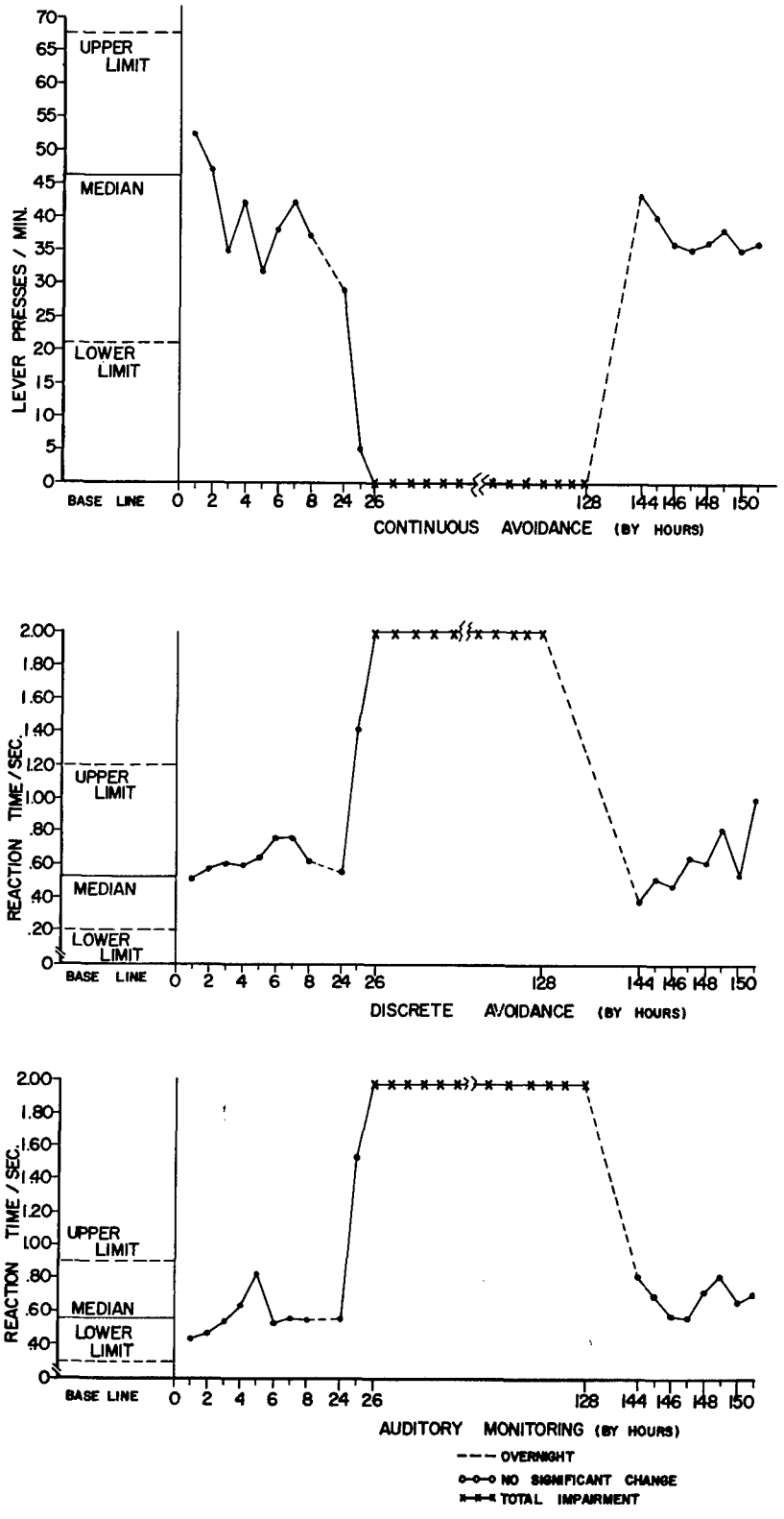

Figure 6. Baseline and Experimental Performance, Subject No. 7

0934 - Is taking CA shock and is refusing to work although he can be alerted. He works awhile and then quits. Subject is vocalizing. Heard the auditory stimulus but pulled the wrong lever and was shocked. Appears to be very confused. Performance on all tasks is now below baseline.

1035 - Sees the visual stimuli but is so confused he cannot make the appropriate response. He continues to hear the auditory stimulus (his ears "perk up" and he moves about) but he cannot make the appropriate response.

1122 - Is bent over, is oblivious to his surroundings, but is easily aroused and appears alert for a few seconds after arousal.

Day 3

0830 - Is in various stages of catatonic behavior with periods of lucidness. Can be aroused at times but may revert to a prone position immediately. During this first work session subject did not work although he was apparently aware of the various stimuli and reacted vociferously to the shock for failure to respond.

0955 - Returned to a head stand position.

1005 - Did not work.

1330 - Is in a head-down, catatonic state.

Day 4

0800 - Will not react to stimuli and will not move toward front of cage.

Day 5

0800 - Refused to enter work chamber and fought efforts to force him into the chamber. After being forced into the work chamber would not work. Ate only about one-half apple last night.

Day 6

0800 - Was difficult to get out of his living cage into the transfer cage. He also was reluctant to get out of his transfer cage into the work chamber.

0930 - Still will not work.

0945 - Can be aroused relatively easy and exhibits some aggressiveness.

Day 7

0905 - Performance looks much better today. He took no shocks the 1st work session (0830-0845).

1600 - Has returned to his baseline level of performance (for last 8 hours work) and will no longer continue in the testing program.

Subject No. 8

Summary of Performance

Performance on CA and AM fell below baseline level at the 49th hour and DA at the 52nd hour. The subject became completely impaired on all tasks at the 53rd hour. The subject began to attempt to respond on DA again at the 72nd hour. Between hours 76 and 144 performance on DA improved and worsened dramatically, but at the 144th hour performance returned to a stable baseline level and was maintained. Performance on CA began again at the 144th hour and from the 145th hour onward was of baseline quality. Auditory Monitoring performance was attempted infrequently between hours 72 and 144, but to little avail. Performance on AM returned to and was maintained at baseline level beginning at the 149th hour. Figure 7 provides a graphic presentation of the significant performance changes when compared with baseline data.

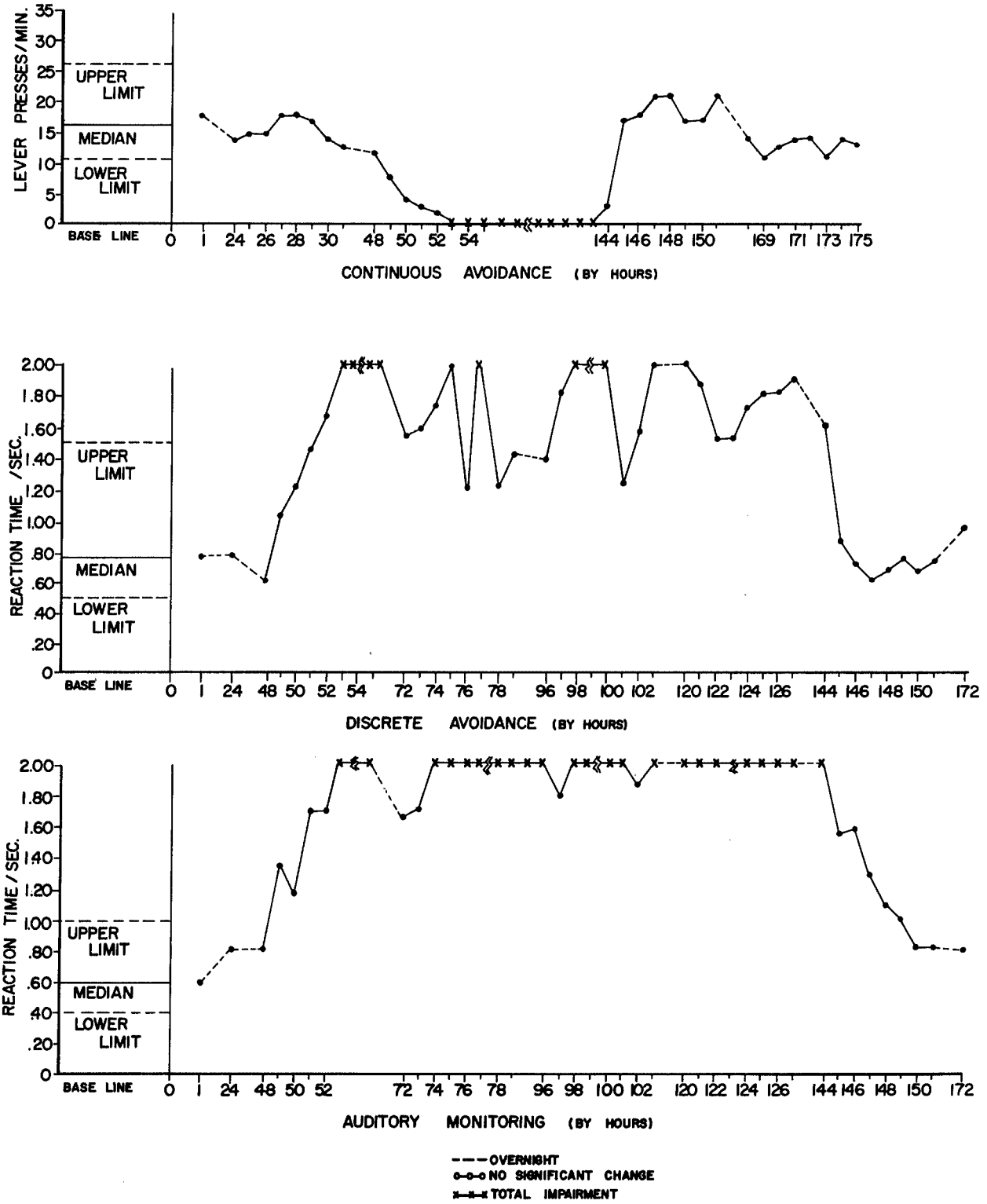

Figure 7. Baseline and Experimental Performance, Subject No. 8

Pertinent Observations

Day 1

1318 - Salivating considerably.

1349 - Going to sleep but easily aroused. Still jumps to implied threat.

Day 2

1515 - No change from yesterday.

Day 3

0930 - Started working fairly well and then circled the cage and took shocks. Worked in spurts and took both CA and AM shocks but performed the DA without shock. Worked in this manner during the first and second sessions.

1005 - Bares teeth when shocked, shakes the bars of the cage, bites the bars and vocalizes. Still tries to hit the AM button. Performance below baseline but still clinically alert. Subject observes movements outside his chamber, appears completely lucid, but is terribly confused.

1100 - Does not react to the performance stimuli; however, he is completely aware of personnel approaching the work chamber.

1330 - Is in a head-down, catatonic state.

Day 4

0800 - Is depressed but will come to front of the cage and grimace when provoked. No work on CA but reacts to DA and AM.

0930 - Performed CA a little, and reacted relatively unsuccessfully to DA and AM. Looks like an animal who is just learning. Vocalizes constantly. Reaction is typical of escape behavior rather than conditioned avoidance.

1012 - Is confused, made one DA lever press but cannot cope with the rest of the performance program. Turned off apparatus after 12 minutes.

1500 - Has tried to perform on four occasions today but took too many shocks and program was turned off.

Day 5

0800 - Readily alerted but has tremors and prefers a huddled position. He is clinically aware but will not work.

1015 - Worked a little.

Day 6

0920 - Did not perform as well from 0900-0915 as he did from 0800-0815.

0945 - Is more easily aroused today and exhibits aggressive responses (baring of teeth and jumping at experimenters).

1000 - Is not responding and still greatly confused.

Day 7

0915 - Is doing much better today in his performance. Took only 12/70 shocks the second work session (0900-0915).

Day 8

1600 - Has returned to baseline performance level and will not be worked any longer.

Subject No. 15 (female)

Summary of Performance

Performance on CA and AM took downward trend soon after injection, with AM falling below baseline at the 5th hour and CA at the 7th hour. DA performance did not drop below baseline until the 24th hour. On

day 2, at the 24th hour performance on all tasks was negligible and by the 26th hour the subject was totally impaired. On day 6 (hour 120) the subject exhibited a noticeable improvement in CA and DA performance but this was sporadic until hours 247 and 243 for CA and DA, respectively, at which time these two tasks were of baseline quality. As the subject recovered from the effects of the decaborane she exhibited escape instead of avoidance behavior to the auditory stimulus by standing on a lever. Since she could escape the shock she simply would not work on AM. Consequently, no measures were available for the recovery period. Figure 8 provides a graphic presentation of the significant performance changes when compared with baseline data.

Pertinent Observations

Day 1

1249 - Lying down, appears to sleep after working from 1230-1245.

1453 - Emesis following 1430-1445 work session.

1645 - Showed a decided downward trend from the 3rd to the 8th hours of performance and this was not at all characteristic of the normal behavior for this subject.

Day 2

0845 - Will not work, performance highly deteriorated. Clinically this subject looks fine and is alert to implied threats.

0855 - Has fixated inappropriately on the CA lever for the past 10 minutes (not pressing and releasing, just holding lever down). No ptosis observed in her and no muscular twitches or fasciculations.

0915 - Still fixated on the CA lever but is alert to implied threats. She is salivating and almost catatonic.

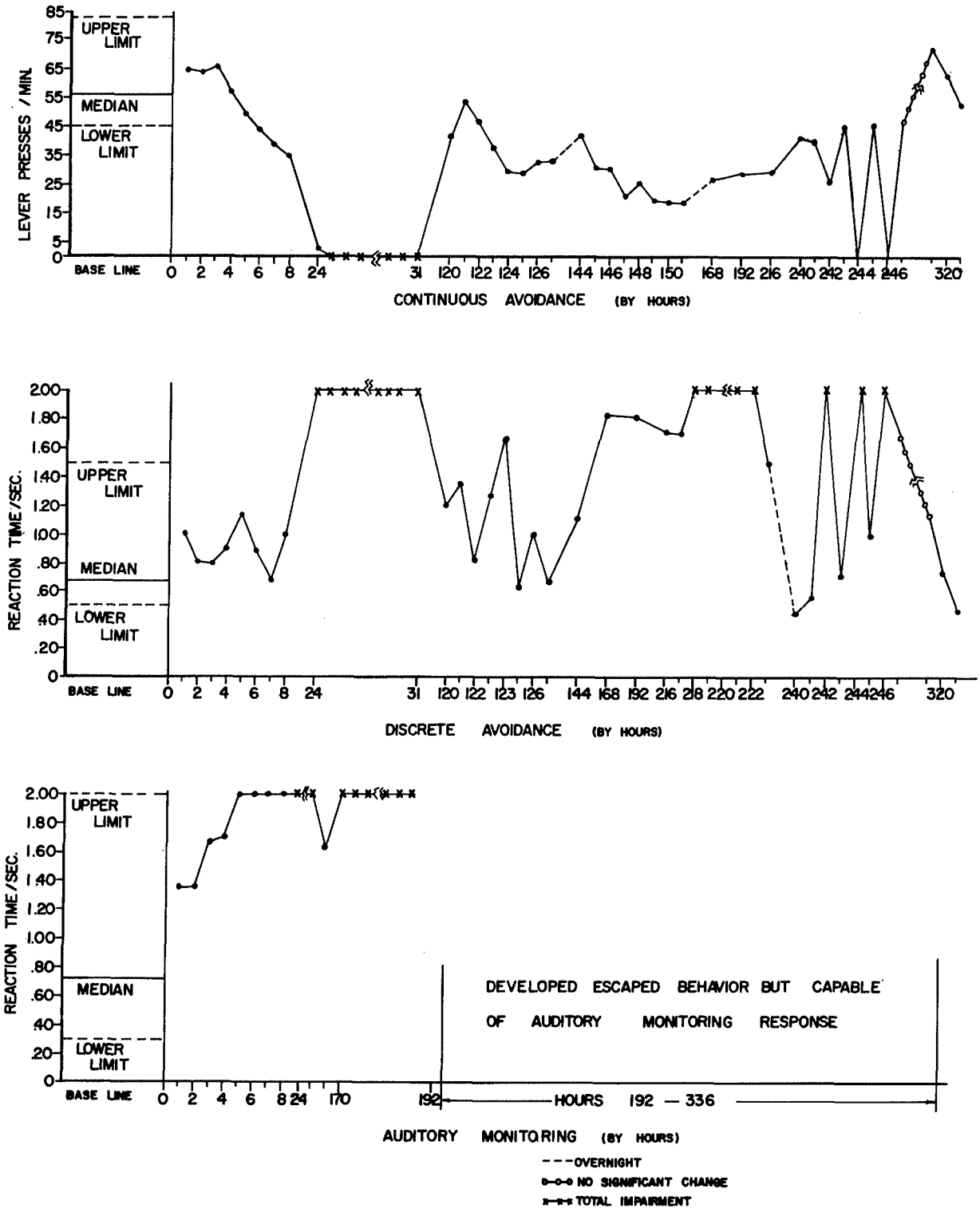

Figure 8. Baseline and Experimental Performance, Subject No. 15

0934 - Taking shock and has not moved from her fixed position on the CA lever. Each time she is shocked she vocalizes or grimaces, appears angry, but does not do anything to alter the situation.

1035 - Has changed positions and jumps off the floor to try to avoid shock.

1122 - In a fixed position and is almost catatonic. She is completely oblivious to her surroundings but can be aroused.

1200 - Has given up completely and is lying on her side. She is essentially unresponsive to external noise or implied threats.

1202 - Got up and assumed a rigid catatonic position by the work panel.

1220 - Is now having muscle twitches and fasciculations.

1300 - Has marked ptosis and is catatonic. Responds to shock only by grimaces and by opening her eyes.

Day 3

0830 - Is in various stages of catatonic behavior with periods of lucidness. Can be aroused at times but may revert to a prone position immediately. During the first work session at 0830 subject did not work at all.

0955 - Taken from work chamber for examination. Subject has a mildly bloody nose and is salivating markedly. Her rectal temperature is 101°. She has marked muscular fasciculations and is hard to handle. Lungs sounded normal, heart clear but quite fast. When replaced in work chamber she went back into a depressed head-stand position.

1005 - Does not work and is just observed for periods of lucidity.

1330 - Is in a head-down, catatonic state. Gazes at the ceiling of her chamber and rolls her head from side-to-side intermittently.

Day 4

0800 - Is much better today, reacts to provocation, but reverts to head-down sitting position when left alone.

1155 - Apparently this subject (the only female) is having a secretion from her mammary glands since a small amount of a milky substance is dripping from these glands.

Day 5

0800 - Moved easily into performance chamber. Has muscular tremors and slight cake of blood on nostrils and upper lip. Will not work.

Day 6

0845 - Is obviously improved over yesterday.

0945 - Still some secretion from mammary glands.

0955 - Performance still improving - a little better than the previous work session.

Day 8

0950 - Attempting to bite herself.

1100 - Lying down as if going to sleep.

1200 - Very agitated. Started off session pounding CA lever, and after first DA began to try to escape.

Day 9

1125 - Biting herself and is highly restless. Behaves very similar to subject No. 22 before he had to be restrained to keep him from injuring himself.

1315 - Is still evasive in her performance (tries to climb up to ceiling when stimuli are presented). Still below base-line performance level.

Day 10

0800 - Entered her work chamber readily and looks clinically sound. Appears to be calm enough this morning and is not trying to injure herself.

1600 - Will continue working until her performance is considered "typical."

Day 11

1600 - Functioning at a very stable level and the experimenters are of the opinion that she has recovered from the effects of the decaborane.

Subject No. 23

Summary of Performance

Performance was depressed following injection but CA did not fall below baseline until the 24th hour and DA the 28th hour. At the 31st hour DA performance became completely impaired followed by CA at the 49th hour. On day 5 (hours 101 to 103) the subject exhibited a noticeable improvement but it was not until day 6 (hour 122) that CA performance could be construed as "normal." DA performance did not return to baseline until the 247th hour. Figure 9 provides a graphic presentation of the significant performance changes when compared with baseline data.

Pertinent Observations

Day 2

0855 - Is much less aggressive today than yesterday (date injected) but clinically normal in appearance.

Day 3

0830 - Is in various stages of catatonic behavior with periods of lucidness. Can be aroused at times but may revert to a

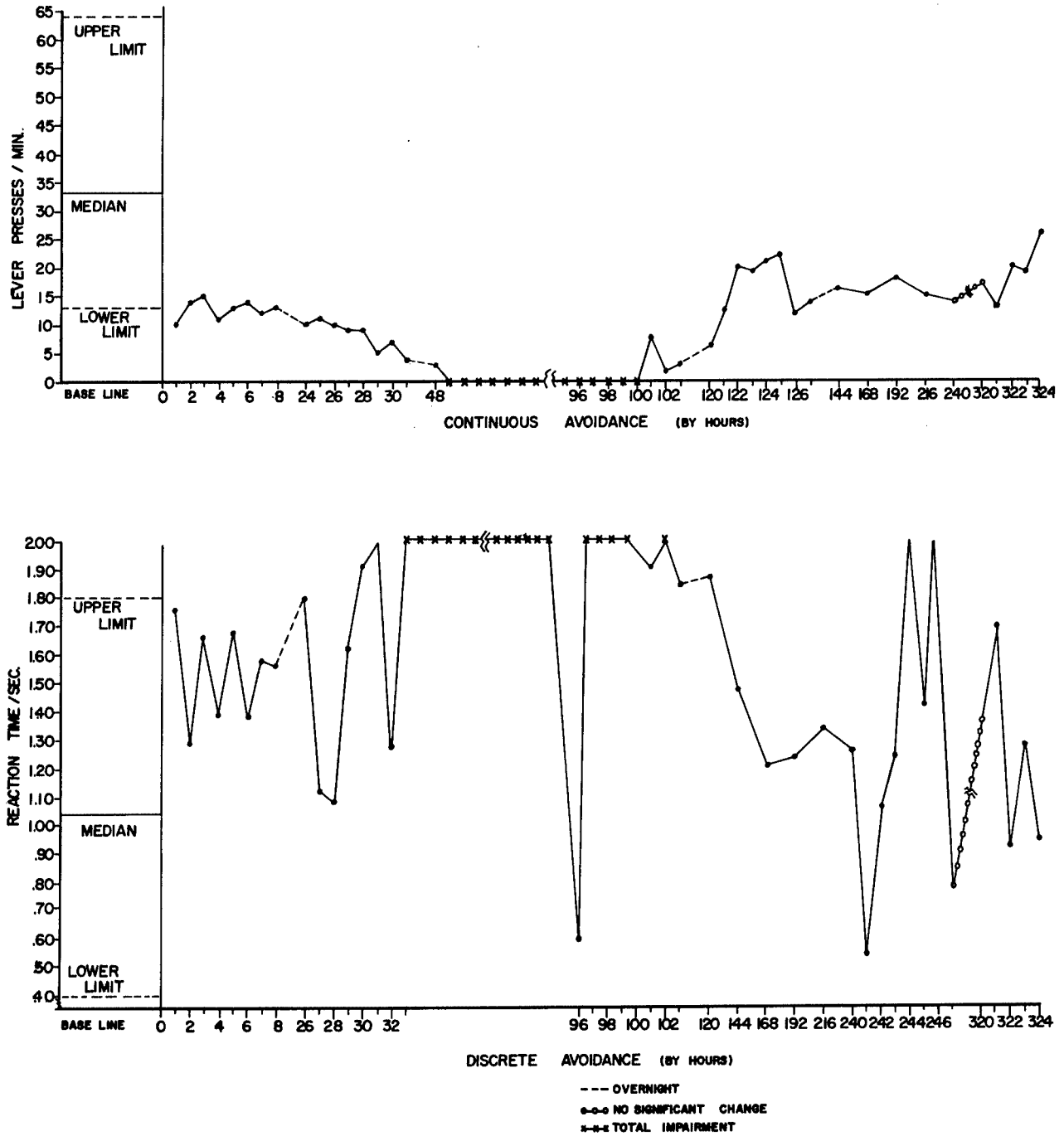

Figure 9. Baseline and Experimental Performance, Subject No. 23

prone position immediately. Worked a little at first and then circled the cage. Tried to get away from failure-to-respond shocks by climbing on the levers. Finally fixated on the CA lever and worked very little thereafter.

0955 - Went back into a depressed head-stand position.

1005 - Did not work and is just observed for periods of lucidity.

1330 - Is in a head-down, catatonic state.

Day 4

0800 - Is somewhat aware of surroundings and will react to external stimuli but then reverts to head-down position.

1010 - Has muscle twitches and fasciculations. Quite alert to noises.

Day 5

0800 - Reluctant to transfer from cage to work chamber and appears withdrawn. Does not work effectively but grabs lever from time to time.

1315 - Is improving and is beginning to look somewhat "normal" again.

Day 9

1315 - DA performance still below baseline.

1600 - Is still below DA baseline performance level and must continue work tomorrow.

Day 10

0800 - Entered work chamber readily and looks clinically sound.

1600 - Is within baseline performance limits.

Day 11

0800 - Decided to "run" subject one more day just to make sure that he is functioning typically.

1600 - Is functioning at a very stable level and the experimenters are of the opinion that he has fully recovered from the effects of the decaborane.

Table II provides a summary of the experimental results, including information on the two subjects that were positively reinforced. The initial hour of onset of clinical symptoms is reported alongside the behavioral data.

IV. DISCUSSION AND CONCLUSIONS

All animals subjected to decaborane injection did show a performance decrement on at least one task. However, two of the Group I subjects (No. 2 and No. 9) did not exhibit a significant decrement at any time on the Discrete Avoidance and Auditory Monitoring, nor did they exhibit any clinical symptoms of sickness. Further, the other two subjects from Group I (No. 4 and No. 22) exhibited performance decrements on all tasks in advance of clinical symptoms. This was also true of two of the Group II subjects (No. 8 and No. 23), as well as the two subjects which were on the positively reinforced discrimination tasks. In only two subjects (No. 7 and No. 15, group II) did clinical symptoms precede performance decrements, and one of these (No. 15) by only one hour.

The results suggest that if a subject does show a decrement below the baseline level on a negatively reinforced task (CA, DA or AM), there will not be a significant difference between the 2 mg and 4 mg exposures as regards time of total impairment, noticeable improvement, and return to baseline performance levels. Those subjects working under positive reinforcement conditions (food reward), which received 1 mg followed by 2 mg the next day, may not show noticeable improvement or return to baseline for a much longer period when compared with the 2-mg and 4-mg groups. This

TABLE II

Summary of Effects of Decaborane (in hours)

Group I (2 mg/kg)

Subject No.	First Clinical Symptoms	Performance Consistently Below Baseline			Total Impairment			Noticeable Improvement			Returned to Baseline		
		CA	DA	AM	CA	DA	AM	CA	DA	AM	CA	DA	AM
2	N/A	48	Never	Never	N/A	N/A	N/A	144	N/A	N/A	170	N/A	N/A
4	96	1	31	29	51	51	51	126	124	125	144	144	144
9	N/A	31	Never	Never	N/A	N/A	N/A	54	N/A	N/A	78	N/A	N/A
22	29	24	28	NT	30	30	NT	120	96	NT	240	120	NT

Group II (4 mg/kg)

7	1	25	25	25	26	27	26	144	144	144	144	144	144
8	53	49	52	49	53	53	53	144	121	145	145	145	149
15	6	7	24	5	26	26	26	120	120	No Data	247	243	No Data
23	48	24	28	NT	49	31	NT	101	103	NT	122	247	NT

Positively Reinforced Subjects (1 mg/kg followed in 24 hours by 2 mg/kg)

Subject No.	First Clinical Symptoms	Performance Consistently Below Baseline	Total Impairment	Noticeable Improvement	Returned to Baseline
2R	96	24	72	216	408
18	72	24	48	192	312

N/A = Not Applicable
NT = Not Trained

seems to suggest that an accurate evaluation of an animal's ability to perform at a given time in a high risk situation may best be achieved by employing negative reinforcement (avoidance of discomfort).

The two key factors - performance changes and clinical symptoms - which may alert responsible personnel to decaborane exposure, must be examined for each of the behavioral tasks employed in this research effort. The relationship between these two factors is presented in table III.

In conclusion, following decaborane injection at the doses used in this research, one may expect 100% of the subjects to show a performance decrement in at least one essential work area, with 75% of the subjects exhibiting a decrement on the remaining tasks. In over half the exposures a change in performance will precede clinical symptoms by a distinctive time period, but in one-fifth of the exposures clinical illness will precede performance changes. In one-twelth of the exposures a performance decrement may occur but there will not be associated clinical illness. And in one-sixth of the cases there will be neither illness nor performance changes.

Personnel who are exposed to the levels of decaborane employed in this study may be expected to exhibit a performance decrement or clinical symptoms in the first 50 hours, since one or the other will probably occur during that time period. Usually, the first indication will be a performance decrement within the first 30 hours on a task requiring continuous motor behavior or a series of discriminations. Tasks of a discrete nature may, at lower exposure levels, reflect no decrement and, in these instances, there may also be a total absence of clinical symptoms. When performance decrements do take place one may expect a return to baseline between 3-10 days.

TABLE III

Relationship Between Performance Changes and Clinical Symptoms

Task	No Illness or Performance Decrement	Illness, but no Performance Decrement	No Illness, but a Performance Decrement	Illness Preceded by Performance Decrement	Illness Followed by a Performance Decrement
CA	0	0	2	4	2
DA	2	0	0	4	2
AM	2	0	0	3	1
Discriminatory	0	0	2	13	5
	4	0	2	13	5
	(≈ 16%)	(0%)	(≈ 8%)	(≈ 54%)	(≈ 21%)

The above values total 24 instances of possible decrements. These 24 instances are derived from 6 subjects x 3 tasks (CA, DA and AM) = 18, 2 subjects x 2 tasks (CA and DA) = 4, and 2 subjects x 1 task (discriminatory) = 2.

REFERENCES

1. Cole, V. V., D. L. Hill, and A. H. Oikemus. "Problems in the Study of Decaborane and Possible Therapy of Its Poisoning." AMA Arch Ind Hyg and Occupational Med, 10, p. 158, 1954.

2. Delgado, J. M. R., K. C. Back, and A. A. Tamas. "The Effect of Boranes on the Monkey Brain." Achives Internationales de Pharmacodynamie et de Therapie, CXL1:262 (1963).

3. Feinsilver, L., L. H. Lawson, P. P. Yevich, and K. H. Jacobson. The Acute Inhalation Toxicity of Several Boron Hydrides. U.S. Army Chemical Warfare Laboratories Technical Report No. 2367, Army Chemical Center, Maryland, March 1960.

4. Krackow, E. H. Toxicity and Health Hazards of Boron Hydrides. U.S. Army Chemical Corps Medical Laboratories Special Report No. 8, Army Chemical Center, Maryland, November 1951.

5. Lowe, H. J. and G. Freeman. "Boron Hydride (Borane) Intoxication in Man." AMA Arch Ind Health, 16, p. 523, 1957.

6. Miller, D. F., A. Tamas, and L. Robinson. A Simple Clinical Test for Boron Hydride Exposure, WADC Technical Report 59-123, Wright Air Development Center, Wright-Patterson Air Force Base, Ohio, April 1959.

7. Miller, D. F., A. Tamas, L. Robinson, and E. Merriweather. "Observations on Experimental Boron Hydride Exposures." Toxicology and Applied Pharmacology, 2, p. 430, 1960.

8. Rozendaal, H. M. "Clinical Observations on the Toxicology of Boron Hydrides." AMA Arch Ind Hyg and Occupational Med, 4, p. 257, 1951.

9. Schoettlin, C.E., G. M. Cinko, R.D. Walter, and T. Freeman. Toxicological Research on Central Nervous System Effects of the Borane Fuels. ASD Technical Report 61-438, Aeronautical Systems Division, Wright-Patterson Air Force Base, Ohio, September 1961.

10. Svirbely, J. L. "Acute Toxicity Studies of Decaborane and Pentaborane by Inhalation." AMA Arch Ind Hyg, 10, p. 298, 1954.

11. Svirbely, J. L. "Subacute Toxicity of Decaborane and Pentaborane Vapors." AMA Arch Ind Hyg, 10, p. 305, 1954.

12. Svirbely, J. L. "Toxicity Tests of Decaborane for Laboratory Animals. I. Acute Toxicity Studies." AMA Arch Ind Health, 11, p. 132, 1955.

13. Svirbely, J. L. "Toxicity Test of Decaborane for Laboratory Animals. II. Effect of Repeated Doses." AMA Arch Ind Health, 11, p. 138, 1955.

14. Tamas, A. A. and Smith, D. L. State of the Art Report on Health Hazards of Borane Fuels and their Control. Aerospace Medical Laboratory, ASD, Wright-Patterson AFB, Ohio, October 1958.

15. Walton, R. P., J. A. Richardson, and L. J. Brodie. "Cardiovascular Actions of Decaborane." Journal of Pharmacology and Experimental Therapeutics, 114, p. 367, 1955.

16. Wills, J. H. Toxicity and Pharmacology of Boron Hydrides. Special Report 15, Chemical Corps Medical Laboratories, Army Chemical Center, Maryland, February 1953.

UNCLASSIFIED

Security Classification

DOCUMENT CONTROL DATA - R&D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)

1. ORIGINATING ACTIVITY *(Corporate author)* 6571st Aeromedical Research Laboratory, Holloman AFB New Mexico, and Aerospace Medical Research Laboratories, Wright-Patterson AFB, Ohio	2a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED 2b. GROUP N/A

3. REPORT TITLE

THE EFFECT OF DECABORANE INJECTION ON MACACA MULATTA AND MACACA IRUS OPERANT BEHAVIOR

4. DESCRIPTIVE NOTES *(Type of report and inclusive dates)*

Final report, 10 February 1964 - 24 February 1964

5. AUTHOR(S) *(Last name, first name, initial)*

Reynolds, Herbert H., Major, USAF; Brunson, Henry W., A2C, USAF; Back, Kenneth C., PhD; and Thomas, Anthony A., MD

6. REPORT DATE	7a. TOTAL NO. OF PAGES	7b. NO. OF REFS
August 1964	42	16

8a. CONTRACT OR GRANT NO. b. PROJECT NO. 6302 c. Task No. 630202 d.	9a. ORIGINATOR'S REPORT NUMBER(S) AMRL-TDR-64-74 9b. OTHER REPORT NO(S) *(Any other numbers that may be assigned this report)* None

10. AVAILABILITY/LIMITATION NOTICES

Qualified requesters may obtain copies of this report from DDC. Available from the Office of Technical Services, Department of Commerce, Washington, D. C. 20230.

11. SUPPLEMENTARY NOTES	12. SPONSORING MILITARY ACTIVITY
None	Aerospace Medical Research Laboratories Wright-Patterson AFB, Ohio

13. ABSTRACT Ten adult monkeys, eight on negatively, and two on positively reinforced tasks, were injected with either 2 mg, 4 mg, or 1 mg followed by 2 mg decaborane per kg body weight. Their performance on various operant tasks was compared with baseline performance. All animals exhibited a performance decrement on at least one task; 75% of the subjects exhibited a decrement on the remaining tasks. In over half the cases performance changes preceded clinical symptoms. There was no significant difference between the 2 and 4 mg exposures when a subject showed a decrement on negatively reinforced tasks. Those subjects that received 1 mg followed the next day by 2 mg (positively reinforced animals) did not noticeably improve or return to baseline for a much longer period than the 2 mg and 4 mg groups (negatively reinforced). Subjects exposed to these levels of decaborane may be expected to exhibit a performance decrement or clinical symptoms during the first 50 hours, since one or the other will probably occur during that time period. At lower exposure levels tasks of a discrete nature may reflect no decrement and clinical symptoms may be absent. When performance decrements do occur one may expect a return to baseline between 3 and 10 days.

DD FORM 1 JAN 64 1473

UNCLASSIFIED

Security Classification

14 KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Psychopharmacology Pharmacology Toxicology Behavior Decaborane Animals						

INSTRUCTIONS

1. ORIGINATING ACTIVITY: Enter the name and address of the contractor, subcontractor, grantee, Department of Defense activity or other organization *(corporate author)* issuing the report.

2*a*. REPORT SECURITY CLASSIFICATION: Enter the overall security classification of the report. Indicate whether "Restricted Data" is included. Marking is to be in accordance with appropriate security regulations.

2*b*. GROUP: Automatic downgrading is specified in DoD Directive 5200.10 and Armed Forces Industrial Manual. Enter the group number. Also, when applicable, show that optional markings have been used for Group 3 and Group 4 as authorized.

3. REPORT TITLE: Enter the complete report title in all capital letters. Titles in all cases should be unclassified. If a meaningful title cannot be selected without classification, show title classification in all capitals in parenthesis immediately following the title.

4. DESCRIPTIVE NOTES: If appropriate, enter the type of report, e.g., interim, progress, summary, annual, or final. Give the inclusive dates when a specific reporting period is covered.

5. AUTHOR(S): Enter the name(s) of author(s) as shown on or in the report. Enter last name, first name, middle initial. If military, show rank and branch of service. The name of the principal author is an absolute minimum requirement.

6. REPORT DATE: Enter the date of the report as day, month, year; or month, year. If more than one date appears on the report, use date of publication.

7*a*. TOTAL NUMBER OF PAGES: The total page count should follow normal pagination procedures, i.e., enter the number of pages containing information.

7*b*. NUMBER OF REFERENCES: Enter the total number of references cited in the report.

8*a*. CONTRACT OR GRANT NUMBER: If appropriate, enter the applicable number of the contract or grant under which the report was written.

8*b*, 8*c*, & 8*d*. PROJECT NUMBER: Enter the appropriate military department identification, such as project number, subproject number, system numbers, task number, etc.

9*a*. ORIGINATOR'S REPORT NUMBER(S): Enter the official report number by which the document will be identified and controlled by the originating activity. This number must be unique to this report.

9*b*. OTHER REPORT NUMBER(S): If the report has been assigned any other report numbers *(either by the originator or by the sponsor)*, also enter this number(s).

10. AVAILABILITY/LIMITATION NOTICES: Enter any limitations on further dissemination of the report, other than those imposed by security classification, using standard statements such as:

(1) "Qualified requesters may obtain copies of this report from DDC."

(2) "Foreign announcement and dissemination of this report by DDC is not authorized."

(3) "U. S. Government agencies may obtain copies of this report directly from DDC. Other qualified DDC users shall request through _____."

(4) "U. S. military agencies may obtain copies of this report directly from DDC. Other qualified users shall request through _____."

(5) "All distribution of this report is controlled. Qualified DDC users shall request through _____."

If the report has been furnished to the Office of Technical Services, Department of Commerce, for sale to the public, indicate this fact and enter the price, if known.

11. SUPPLEMENTARY NOTES: Use for additional explanatory notes.

12. SPONSORING MILITARY ACTIVITY: Enter the name of the departmental project office or laboratory sponsoring *(paying for)* the research and development. Include address.

13. ABSTRACT: Enter an abstract giving a brief and factual summary of the document indicative of the report, even though it may also appear elsewhere in the body of the technical report. If additional space is required a continuation sheet shall be attached.

It is highly desirable that the abstract of classified reports be unclassified. Each paragraph of the abstract shall end with an indication of the military security classification of the information in the paragraph, represented as *(TS), (S), (C), or (U)*

There is no limitation on the length of the abstract. However, the suggested length is from 150 to 225 words.

14. KEY WORDS: Key words are technically meaningful terms or short phrases that characterize a report and may be used as index entries for cataloging the report. Key words must be selected so that no security classification is required. Identifiers, such as equipment model designation, trade name, military project code name, geographic location, may be used as key words but will be followed by an indication of technical context. The assignment of links, rules, and weights is optional.